e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(10); 182-186

Original Research Article

A Hospital-Based Study Assessing the Effect of Duration of Disease and Glycemic Control on Attention, Executive Function and Visual Reaction Time in Type 2 Diabetes Mellitus Patients

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Received: 22-07-2023 Revised: 26-08-2023 / Accepted: 08-09-2023
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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to correlate duration of disease with attention, executive function and visual reaction time in type 2 diabetes patients and to correlate HbA1c with attention, executive function and visual reaction time in type 2 diabetes patients.

Methods: This is a cross-sectional study done on 50 type 2 diabetes mellitus subjects of either sex under the age group of 40-60 years in the Department of Physiology for 12 months . The subjects who are able to understand English were enrolled for the study. Written informed consent was taken and each subject was explained about the whole procedure and objective of the study.

Results: The mean age and BMI of the patients were 56.04±4.46 and 25.55+1.96 respectively. There were 28 male and 22 females in the present study. Duration of disease was positively correlated (r=0.32) with score of Digit Vigilance Test and p value statistically significant (0.012). A positive correlation (r=0.22) was also seen with Visual Reaction time and p value statistically significant (0.042). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance. HbA1c was positively correlated(r=0.58) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.32) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance.

Conclusion: With increase in duration of the disease and poor glycemic control, sustained attention and executive functions are declining. Also there is an increase in visual reaction time. Diabetes is a disease which requires proper self-care and monitoring. The decline in cognitive functions can affect their activities like glucose monitoring, medications or insulin injection patterns, diet and exercise timing.

Keywords: Type 2 Diabetes mellitus, Attention, Executive functions, Reaction time, HbA1c

Introduction

Type 2 diabetes is a chronic metabolic disorder characterized by progressive insulin resistance that is often accompanied by a collection of comorbid conditions, many of which are also progressive. Common comorbid conditions include retinopathy, micro- and macro-vascular disease, peripheral neuropathy, and nephropathy. Previous studies have also found significant cognitive and neural deficits in people with type 2 diabetes. Specific cognitive domains affected include memory, attention, and executive functioning, with effect sizes ranging from 0.25–0.5 [1,2], although moderate to large effect sizes have been found in people over 65 years-old [3], suggesting these decrements increase with aging.

Executive functioning is one cognitive domain particularly affected in type 2 diabetes. [1,2] One task known to tap executive function is task switching, which requires participants to flexibly adjust goal sets and behavior to match contextual cues. [4] Behaviorally, switching rule sets requires longer reaction times relative to stay or no switch trial types, revealing a consistent behavioral switch cost. [5] These paradigms have generally been found to elicit activity across the frontal-parietal and cingulo-opercular networks. [6] While studies have shown that type 2 diabetes affects executive

function, whether the driving force behind these deficits is primarily related to dysglycemia or the increased number of comorbid conditions in those with type 2 diabetes remains to be elucidated. Studies have found mediating effects of high body mass index, age, microvascular damage, and hypertension, as well as glycated hemoglobin (HbA1c) and other metrics of glycemic control on the cognitive decrements associated with type 2 diabetes. [1,7,8] Insulin resistance, a hallmark of the disease, has a direct impact on the brain. Insulin receptors are found across the cortex and subcortical structures including the hippocampus, hypothalamus, and amygdala [9,10] and insulin signaling has been implicated in several cognitive processes, most notably episodic memory performance. [10]

Auditory and visual Reaction time is considered as an ideal tool for measuring sensory motor association and performance of an individual. There is a direct relationship between elevated levels of HbA1C & Diabetic Neuropathy has been reported in Type-II DM. [11,12] In chronic Type-II DM, slowing of reaction time may affect balance leads to probability of slip, fractures, non-healing ulcer which ends in amputation of limbs and disability. Screening for Neuropathy earlier before it manifests clinically by assessing the relationship between the HbA1C& Reaction time becomes mandatory.

The aim of the present study was to correlate duration of disease with attention, executive function and visual reaction time in type 2 diabetes patients and to correlate HbA1c with attention, executive function and visual reaction time in type 2 diabetes patients.

Materials and Methods

This was a cross-sectional study done on 50 type 2 diabetes mellitus subjects of either sex under the age group of 40-60 years in the Department of Physiology, JNKTMCH, Madhepura, Bihar, India for 12 months. The subjects who are able to understand English were enrolled for the study. Written informed consent was taken and each subject was explained about the whole procedure and objective of the study.

A detailed history taking and relevant clinical examination was done for all subjects. Following which, subjects who had hypertension, dyslipidaemia, and any diabetic complications were excluded. Also, diabetic subjects on insulin, those with visual disturbances were excluded. Fasting venous blood samples (2ml) were taken for estimation of HbA1c. HbA1c is measured in BIORAD D-10 machine using latex agglutination inhibition assay. Cognitive tests that measured performances in specific domains of interest were chosen. This includes Digit Vigilance Test (DVT) for attention and Stroop Test for executive functions. Visual Reaction Time, a measure of attention and fine motor skills were also considered.

Digit Vigilance Test: DVT was administered according to the instructions provided in Neuropsychology Battery7. This test consists of numbers 1-9 arranged randomly and placed in rows in a sheet. Digits are closely packed on the sheet in 50 rows and 30 digits per row. The subject is instructed to cancel the digits 6 and 9 as fast as possible without missing targets or cancelling wrong numbers. Time taken for completion of the test forms the score and was noted using a stopwatch. Lower score indicate better sustained attention.

Stroop test: This test was administered according to the instructions provided in Neuropsychology Battery7. The test consist of a paper in which the colour names Blue, Green, Red, Yellow are printed. Colour of the print occasionally corresponds with the colour designed by the word. There are 16 rows and 11 columns. The subject is instructed to read the words column wise as fast as possible. Time taken to read all the 11 columns were noted down using stopwatch. Next the subject was asked to name the colour in which the word was printed. The time taken to name all the colours in the column wise was also noted. Reading time and naming time were converted into seconds. Reading time was subtracted from naming time to get the Stoop effect score. Lower score indicates better executive functions.

Visual Reaction Time: VRT was assessed using Human Benchmark Software8. This software consist of a red coloured screen on the laptop monitor. The subject is instructed to focus on the screen and when the red colour changes to green colour, he/she should press the enter key on the keyboard. Five trials were given and average time was taken as the visual reaction time. Lower the reaction time better is the attention and fine motor skills.

Statistics: Data presented as Mean + Standard deviation. Pearson correlation was used to correlate duration of disease and HbA1c on attention, executive function and visual reaction time. P value <0.05 was considered statistically significant. Statistical analysis was done using Microsoft Excel 2013.

Results

Table 1: Demographic details of the study group

Parameters	Study group
Age (yrs.)	56.04±4.46
BMI (kg/m2)	25.55+1.96
Male	28
Female	22

The mean age and BMI of the patients were 56.04±4.46 and 25.55+1.96 respectively. There were 28 male and 22 females in the present study.

Table 2: Correlation between duration of disease and different tests

Test	r	p value
DVT	0.32	0.012
VRT	0.22	0.042
STROOPTEST	0.15	0.260

Here, duration of disease was positively correlated (r=0.32) with score of Digit Vigilance Test and p value statistically significant (0.012). A positive correlation (r=0.22) was also seen with Visual Reaction time and p value statistically significant (0.042). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance.

Table 3: Correlation between HbA1c and different test

Test	r	p value
DVT	0.58	0.01
VRT	0.32	0.01
STROOP TEST	0.15	0.34

HbA1c was positively correlated(r=0.58) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.32) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance.

Discussion

Type 2 diabetes mellitus is a common endocrine disorder [13] and is on constant rise in the world. [14] Diabetes mellitus is associated with premature mortality [15] and several complications such as neuropathy, nephropathy and cardiovascular disease. [13] It can also affect brain leading to accelerated cognitive decline and an increased risk of dementia. [16] In Cardiovascular Health Study, the prevalence of mild cognitive impairment was 19% in individuals of age > 65years and 29% in those aged >85years. [15] Cognitive decline can be seen in both type 1 and type 2 diabetes mellitus patients, but the affected domains remain distinct in these two types with executive functions, memory, learning, attention and psychomotor efficiency being more affected in type 2 diabetes mellitus patients. In diabetes patients, the executive functions are particularly important as they involve behaviours, such as insight into a particular problem, problem- solving, judgment, stopping or changing old behaviours and starting new habits, thus affecting the individual's self-care. [17]

The mean age and BMI of the patients were 56.04±4.46 and 25.55+1.96 respectively. There were 28 male and 22 females in the present study. Cognitive alterations, in the form of longer reaction times and impaired spatial planning, occur in diabetic patients. These impairments however, were unrelated to glycemic control, reflected by HbA1C levels, complications and duration of disease. [18] In a systematic analysis it has been reported that hyperglycemia is associated with impaired cognitive functions. [19] Patients with T2DM, regardless of their insulin treatment status have shown higher fatigue scores and cognitive impairment with significant prolongation of reaction times and defective spatial planning. [20]

Duration of disease was positively correlated (r=0.32) with score of Digit Vigilance Test and p value statistically significant (0.012). A positive correlation (r=0.22) was also seen with Visual Reaction time and p value statistically significant (0.042). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance. HbA1c was positively correlated (r=0.58) with the score of Digit Vigilance Test and p value statistically significant (0.01). A positive correlation (r=0.32) was also seen with Visual Reaction time and p value statistically significant (0.01). Stroop test score also shows a positive correlation (r=0.15) but without any statistical significance. Sustained attention was tested by DVT. It refers to the capacity to attend a task for a required period of time. Right fronto-parietal network mediates sustained attention. Executive functions tested by Stroop test indicate Response inhibition by the brain. Response Inhibition measures the ease with which a perceptual set can

be shifted both to conjoin changing demands and by suppressing a habitual response in favour of an unusual one. Pre-frontal areas are essential for response inhibition.[21] Visual reaction time was tested for attention and fine motor skills. It indicates the time taken for processing of sensory stimulus by central nervous system and its execution in the form of motor response. [14]

Glucose serves as a fuel for the brain and is necessary for cognitive performances. Hyperglycemia alters the cognitive functions through a variety of mechanisms like, polyol pathway activation, increased formation of Advanced Glycated End products (AGEs), diacylglycerol activation of protein kinase C and increased glucose shunting in the hexosamine pathway. Hyperglycemia decreases the glucose availability to the brain by impairing the transfer of glucose across the Blood-Brain-Barrier and between the intra and extracellular fluids in the brain, thus impacting cognitive performance. Even a reduction in availability of acetylcholine caused by decrease transport of glucose across the BBB is attributed to cognitive decline. [22] Diabetes Mellitus affects the peripheral nerves in the somatosensory and auditory system, slows psychomotor responses and has cognitive effects all of which may affect reaction times. Some studies states that axonal degeneration of both myelinated and unmyelinated fibres, axon shrinkage, axon fragmentation, thickening of basement membrane and micro thrombi delays motor nerve conduction velocity, thus delaying the reaction time. [14]

Conclusion

Type 2 diabetes mellitus is a risk factor for cognitive impairment. In the present study, HbA1c which is a marker of chronic hyperglycemia and duration of disease are correlated with few cognitive domains like attention, executive function and reaction time. With increase in duration of the disease and poor glycemic control, sustained attention and executive functions are declining. Also there is an increase in visual reaction time. Diabetes is a disease which requires proper self-care and monitoring. The decline in cognitive functions can affect their activities like glucose monitoring, medications or insulin injection patterns, diet and exercise timing. Hence identification of cognitive impairments and their relation with Diabetes is an important step for prevention of cognitive decline.

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